II. REMARKS

Formal Matters

Claims 1, 2, 6-14, 16-18, 20-22, and 25-29 are pending after entry of the amendments set forth herein.

Claims 1, 2, 6-18, 20-22, 25, and 26 were examined and were rejected.

Claim 15 is canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claim. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Claims 27-29 are added. Support for new claims 27-29 is found in the claims as originally filed, and throughout the specification, including the following exemplary location: paragraph 0072. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Withdrawn rejections

Applicants note with gratitude that the following rejections, raised in the July 21, 2009 Office Action, have been withdrawn:

i) rejection of claims 1, 2, and 6-25 under 35 U.S.C. §112, second paragraph;

ii) all rejections under 35 U.S.C. §112, first paragraph; and

iii) claims 22-25 under 35 U.S.C. §103(a) as allegedly unpatentable over Schneider, Yang, Kumar, and Bujard, and further in view of Sedegah.

Examiner Interview

The undersigned Applicants' representative thanks Examiner Zacharia Lucas for the courtesy of an in-person interview which took place on February 23, 2009, and which was attended by Examiner Lucas and Applicants' representative Paula A. Borden.

During the interview, the rejections were generally discussed. The undersigned Applicants' representative thanks Examiner Lucas for the indication of willingness to hold a further interview.

Objection to the specification

The Office Action stated that the specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. The Office Action acknowledged that there is written description support for the claim language regarding vaccines that "do not comprise an adjuvant"; and requested that Applicants insert antecedent basis support for such language.

As discussed in the amendment, filed on November 23, 2009 and responsive to the July 21, 2009 Office Action, the instant specification provides adequate written description support for the recitation in claim 20 "wherein the vaccine does not comprise an adjuvant."

As discussed in the November 23, 2009 amendment, in the protocol and results described in paragraphs 0084-0098, no adjuvant was used. Thus, these paragraphs provide adequate support for the phrase "wherein the vaccine does not comprise an adjuvant." It is noted that the paragraphs describing the experiments and results relating to Figures 3A and 3B note that in some instances, an adjuvant was used. Thus, where no adjuvant is mentioned, no adjuvant was used. It is standard, where a vaccination protocol is described, to indicate when an adjuvant is used. It is not standard to indicate what is missing from a solution.

As indicated in paragraphs 0084-0098, no adjuvant was used. As such, the instant specification provides support for the phrase "wherein the vaccine does not comprise an adjuvant."

The current Office Action acknowledged that written description support is present. As such, there does not appear to be any need to amend the specification.

Rejections under 35 U.S.C. §112, second paragraph

Claims 10, 14, and 15 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Claim 10

Claim 10 recites "wherein the signal sequence controls the glycosylphosphatidylinositol anchoring of the at least one fragment of MSP-1." The Office Action stated that the teachings in the art indicate that such a signal sequence is required for the protein to be so attached to a cell membrane. The Office Action cited Yang et al. (1999) *Glycobiol.* 9:1347; "Yang Glycobiology"); and stated that Yang Glycobiology teaches that in addition to the N-terminal signal sequence, a C-terminal GPI anchor (GA) signal is also required. The Office Action stated that it is not clear if claim 10 is suggesting that the signal sequence alone is capable of causing GPI anchoring of the protein. Applicants respectfully traverse the rejection.

As set forth in MPEP §2173.02, definiteness of claim language must be analyzed in light of:

a) the content of the disclosure of the patent application;

b) the teachings of the prior art; and

c) the claim interpretation that would be given by one possessing the ordinary level of skill in the art at

the time the invention was made.

Yang Glycobiology does not appear to indicate that "an additional C-terminal GPI anchor (GA) signal sequence is also required", as the Office Action asserts. Yang Glycobiology discusses constructs encoding the 70-kDa C-terminal polypeptide of *P. falciparum* MSP-1, with or without MPS-1 N-terminal signal peptide and C-terminal GPI anchor signal sequences; and expressing the constructs in the mammalian cell lines monkey kidney SV-1 cells, human Hu134TK$^-$, and HeLa. Yang Glycobiology indicates that the *P. falciparum* MSP-1 GPI anchor signal sequence is either nonfunctional or very poorly functional in the mammalian cell lines studied. However, Yang Glycobiology states that the MSP-1 polypeptide encoded by construct P1, which includes an N-terminal signal sequence and lacks a GPI anchor sequence, **was in fact expressed on the cell surface**. Yang Glycobiology, page 1351, bridging paragraph, columns 1 and 2. As such, Yang Glycobiology does not indicate that "an additional C-terminal GPI anchor (GA) signal sequence is also required", as the Office Action asserts.

Those skilled in the art would understand the meaning of claim 10. As such, claim 10 is clear and need not be amended.

Claims 14 and 15

The Office Action stated that claim 15 indicates that the components (a) and (c) of claim 14 may be administered simultaneously, sequentially, or separately; and stated that if the compounds are part of the same vaccine composition, it is not clear how they can be administered sequentially or separately.

Without conceding as to the correctness of this rejection, claim 15 is cancelled without prejudice to renewal. Claim 14 merely recites an additional component of the vaccine of claim 13. As such, claim 14 is in compliance with the requirements of 35 U.S.C. §112, second paragraph.

Conclusion as to the rejections under 35 U.S.C. §112, second paragraph

Applicants submit that the rejection of claims 10, 14, and 15 under 35 U.S.C. §112, second paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejections under 35 U.S.C. §103(a)

Claims 1, 2, and 6-18, and 22-25 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Schneider et al. ((1998) *Nat. Med.* 4:397; "Schneider") in view of Yang et al. ((1997) *Vaccine* 15:1303-1313; "Yang"), Kumar et al (April, 2002) *Immunology Letters* 81:13-24), and Bujard et al. (WO 98/14583; "Bujard").

Applicants note that claims 23 and 24 were cancelled without prejudice to renewal in the amendment, filed on November 23, 2009 and responsive to the July 21, 2009 Office Action.

The Office Action stated that "it would have been obvious to those of ordinary skill in the art to use p42 antigen identified as a protective antigen in Kumar as the encoded antigen in the plasmid DNA priming/MVA boosting technique suggested by the teachings of Kumar and Schneider." Office Action, page 8. Applicants respectfully traverse the rejection.

The cited art does not disclose or suggest all of the claim limitations.

As described below, the cited art, taken together, does not disclose or suggest all of the claim limitations of claim 1. For example, the cited art does not disclose or suggest a recombinant MVA virus comprising at least one nucleic acid coding for: i) *Plasmodium falciparum* MSP-1 p42; ii) *Plasmodium falciparum* MSP-1 p42 and -38; or iii) *Plasmodium falciparum* MSP-1 p83, p30, p42, and p38.

Schneider

As discussed amply in the November 23, 2009 response[1], **Schneider**, which is the primary reference, discusses **sporozoite** antigens, **not merozoite** antigens.

Schneider discusses Plasmodium species that are not relevant to human malaria.

As discussed in the instant specification, there are four malaria species that infect humans: *Plasmodium malariae*, *Plasmodium vivax*, *Plasmodium ovale*, and *Plasmodium falciparum*, with *Plasmodium falciparum* being responsible for almost all fatal infections. Specification, paragraph 0004.

Schneider relates to immunization of mice with antigens (other than MSP-1) from *Plasmodium berghei*. *Plasmodium berghei* does not infect humans; instead, *Plasmodium berghei* is used to generate models of rodent malaria. Schneider, page 397, column 1, second paragraph. **Schneider is thus not relevant to a recombinant virus comprising a nucleic acid encoding *Plasmodium falciparum* antigens.**

Schneider discusses Plasmodium antigens that are not merozoite surface proteins.

When an individual is bitten by a mosquito that carries malaria, sporozoites present in the material injected into the individual by the mosquito enter the bloodstream of the individual and migrate to the liver.

[1] The "November 23, 2009 response" is the amendment, filed on November 23, 2009 and responsive to the July 21, 2009

Sporozoites infect liver cells, where they multiply into merozoites, rupture the liver cells, and escape back into the bloodstream. Merozoites in the bloodstream infect red blood cells, where they develop into ring forms, then trophozoites (a feeding stage), then schizonts (a reproduction stage), then back into merozoites.

Schneider discusses use of plasmid DNA or MVA vectors encoding *Plasmodium berghei* pre-erythrocytic antigens (thromobspondin-related adhesive protein (**PbTRAP**) and the circumsporozoite protein (**PbCSP**)) to immunize mice against challenge. Both the TRAP and the circumsporozoite proteins are **sporozoite** stage proteins.

The MSP-1 complex of *P. falciparum* constitutes a major component at the surface of the erythrocyte-invading (**merozoite**) form of the parasite.

Thus, Schneider relates to proteins from a different stage of the *Plasmodium* life cycle than MSP-1.

Schneider indicates that use of MVA is not always successful in inducing protective immunity.

Schneider states that various prime-boost immunization strategies, with combination of various recombinant vaccinia virus strains and plasmid DNA, were tested for immunogenicity and protective efficacy. Schneider, page 397, column 2, first full paragraph. Schneider states that using plasmid DNA priming an recombinant MVA boosting, complete protection against sporozoite challenge was observed in two different mouse strains. Schneider states that "[t]his specific order of immunization **was essential for protection**." Schneider, page 397, column 2, first full paragraph, emphasis added. As shown in Table 1a of Schneider, use of MVA encoding PbCSP and PbTRAP for the first (priming) and second (boosting) immunizations resulted in very low protection; and use of MVA encoding PbCSP and PbTRAP for the first immunization, followed by use of plasmid DNA encoding PbCSP and PbTRAP for the second immunization, resulted in **no** protection.

Schneider noted that studies carried out in chimpanzee also involved priming with DNA (i.e., plasmid DNA encoding PbCSP and PbTRAP), followed by boosting with MVA (i.e., MVA encoding PbCSP and PbTRAP).

Thus, not only does Schneider not disclose or suggest all of the features of claim 1, Schneider in fact teaches away from use of MVA as a suitable vector for *P. falciparum* antigens.

Kumar

Also as discussed in the November 23, 2009 response, **Kumar** discusses preparation of a DNA plasmid (**not a virus**) encoding the C-terminal 42-kDa region of merozoite surface protein 1 ($pMSP1_{42}$), and preparation of a recombinant vaccinia virus vector encoding the same C-terminal 42-kDa region.

The data contained in Kumar relate to the effect of **immunization with a DNA plasmid encoding MSP-1 p42** ($pMSP1_{42}$). Kumar, bridging sentence, pages 14-15; and page 15, column 1, section 2.1.1. under "Materials and Methods." In connection with the recombinant vaccinia virus (which was not MVA) construct encoding the same C-terminal 42-kDa region, Kumar states that this recombinant vaccina virus was used **to infect target cells for CTL analysis**. Kumar, page 15, column 2, section 2.2 under "Materials and Methods."

Yang

Yang discusses use of a recombinant vaccinia virus encoding a 190 kDa merozoite surface antigen, with or without anchor and signal sequences. Yang **does not disclose or suggest any recombinant virus encoding *fragments* of MSP-1**.

Yang neither discloses nor suggests:

- a recombinant **MVA virus** comprising at least one nucleic acid coding for a *Plasmodium falciparum* antigen;
- a recombinant MVA virus comprising at least one nucleic acid coding for **at least one fragment** of *P. falciparum* MSP-1, where the at least one fragment is selected from: **i) p42; ii) p42 and p38; and iii) p83, p30, p42, and p38**.

The Office Action stated that the merozoite antigen is processed into fragments (30, 38, and 42 kDa), and stated that each gene was inserted into the thymidine kinase region of the vaccinia virus. Office Action, bridging sentence, pages 10 and 11. The Office Action appeared to imply that genes encoding the 30, 38, and 42 kDa fragments were inserted into the vaccinia virus in Yang. **They were not**.

Yang discusses a recombinant vaccinia virus encoding a C-terminal fragment (**amino acids 1047-1640**) region of MSP-1. Yang, page 1304, column 1, last 8 lines of first full paragraph.

> erythrocytes[26]. An anti-idiotype antibody derived from 2B10 recognized the C-terminal (1047-1640aa) region of MSA1 in a Western blot[26] and appears to recognize the same site on glycophorin A as the merozoite. Here we describe the effect of signal and anchor sequences on the biochemical processing and antibody response to this C-terminal region of MSA1 when expressed by a rVV.

Yang states that the C-terminal fragment is encoded by nucleotides 3553-5280 of the sequence set forth in GenBank Accession No. X02919. Yang, Table 1 and legend. As shown in Exhibit 1,[2] nucleotides 3553-5280 of the X02919 sequence encode amino acids 1047-1621 of MSP-1. As shown in Figure 1 of the instant application, and as depicted schematically in Figure 6A of Kauth et al. (2003) *J. Biol. Chem.* 278:22257, amino acids 1047-1621 of MSP-1 **does not correspond to any of the MSP-1 fragments recited in claim 1**. Instead, as shown in Exhibit 2,[3] amino acids 1047-1621 of MSP-1 begins within p38 and includes most of the amino acid sequence of p42. Thus, Yang discusses a fragment that is not p42, p38, p30, or p83.

Yang does not disclose or suggest a recombinant MVA virus comprising a nucleic acid encoding the particular recited fragments of *P. falciparum*.

Yang mentions in passing that MVA has been developed as an expression vector and shown to be equivalent to replication competent vaccinia virus in several vaccine models.

However, one cannot necessarily extrapolate from vaccinia virus to MVA. First, as noted previously, MVA is highly attenuated, compared to vaccinia virus. It was not necessarily predictable, based on the results of Yang with vaccinia virus, that recombinant MVA comprising a nucleic acid encoding fragments of *Plasmodium falciparum* MSP-1 would be efficacious.

Indeed, Schneider indicated that recombinant MVA encoding *P. berghei* pre-erythrocytic antigens, when administered to mice, in some instances provided no protection at all against challenge.

Bujard

Bujard is entitled "Method for producing recombinants intended for use in a complete malaria antigen GP190/MSP1." Bujard discusses a nucleic acid encoding the complete malaria antigen, where the nucleic acid has a reduced AT content relative to wild-type sequence.

Bujard neither discloses nor suggests:

- a **recombinant MVA virus** comprising at least one nucleic acid coding for a *Plasmodium falciparum* antigen;
- a recombinant MVA virus comprising at least one nucleic acid coding for **at least one fragment**

[2] Exhibit 1 was provided along with the amendment, filed on November 23, 2009 and responsive to the July 21, 2009 Office Action. A copy is provided herewith as a courtesy.
[3] Exhibit 2 was provided along with the amendment, filed on November 23, 2009 and responsive to the July 21, 2009 Office Action. A copy is provided herewith as a courtesy.

of *P. falciparum* MSP-1, where the at least one fragment is selected from: **i) p42; ii) p42 and p38; and iii) p83, p30, p42, and p38**.

The Office Action has mischaracterized the cited art.

The Office Action stated that "each of the Kumar and Schneider references teach the use of vaccinia virus vectors as effective boosters for prior primary administrations of other anti-malarial vaccines" and that Kumar "does teach the use of viral vectors for the purpose of boosting a primary administration of different antigenic composition, such as a plasmid vaccine." Office Action, page 7; and bridging sentence, pages 7 and 8. However, this is a mischaracterization of the cited art.

Kumar does **not** teach "the use of vaccinia virus vectors as effective boosters for prior primary administrations of other anti-malarial vaccines" as asserted in the Office Action.

The only immunizations discussed in Kumar were with **plasmid** DNA encoding MSP-1 p42. Kumar, bridging sentence, pages 14-15; and page 15, column 1, section 2.1.1. under "Materials and Methods."

Kumar used a recombinant vaccinia virus (which was not MVA) construct encoding the same C-terminal 42-kDa region in an *in vitro* assay **to infect target cells for CTL analysis**. Kumar, page 15, column 2, section 2.2 under "Materials and Methods."

Furthermore, the only discussion in Kumar that relates to "the use of viral vectors for the purpose of boosting a primary administration of different antigenic composition, such as a plasmid vaccine" is in the general discussion, e.g., the Introduction (Kumar, page 14, column 2, paragraphs 2 and 3). Kumar states that one way of improving an immune response to a DNA vaccine is to first prime by immunizing with DNA, followed by exposure to antigen. Kumar states that two experiments were conducted: 1) a plasmid encoding the rhesus GM-CSF protein, mixed with a DNA plasmid encoding *P. falciparum* $MSP1_{42}$ was used; and 2) a DNA plasmid encoding *P. falciparum* $MSP1_{42}$ in combination with recombinant human GM-CSF was used. Kumar **does not provide any experiments showing the use of viral vectors for the purpose of boosting a primary administration of different antigenic composition, such as a plasmid vaccine**.

One cannot necessarily extrapolate from vaccinia virus to MVA.

The Office Action appears to be of the position that it would be obvious to substitute MVA for vaccinia virus. However, one cannot necessarily extrapolate from vaccinia virus to MVA. First, as noted previously, MVA is highly attenuated, compared to vaccinia virus. It was not necessarily predictable, based on the results of Yang

with vaccinia virus, that recombinant MVA comprising a nucleic acid encoding fragments of *Plasmodium falciparum* MSP-1 would be efficacious.

Indeed, Schneider indicated that recombinant MVA encoding *P. berghei* pre-erythrocytic antigens, when administered to mice, in some instances provided no protection at all against challenge.

The Office Action has not established a prima facie case of obviousness.

As noted above, the cited art does not disclose or suggest all of the claim elements as recited in claim 1. Furthermore, in contrast to the Office Actions' assertions, the cited art does not provide motivation to make the modification suggested in the Office Action, because the references do not "teach a successful vaccine" where the vaccine would comprise a recombinant MVA comprising a nucleic acid encoding at least one fragment of *P. falciparum*.

As noted above, Schneider teaches that a recombinant MVA encoding *P. berghei* pre-erythrocytic antigens (thromobspondin-related adhesive protein and the circumsporozoite protein) in some instances **failed to induce protective immunity in mice**. As such, one skilled in the art, given Schneider, would **not** have had a reasonable expectation of success, as asserted in the Office Action. Therefore, recombinant MVA vector as claimed, or a vaccine composition comprising same, is **not** simply a predictable combination of prior art elements.

Furthermore, none of the cited art teaches or suggests a recombinant MVA virus comprising a nucleic acid encoding the MSP-1 fragments recited in claim 1. Schneider does not even discuss MSP-1 or any other merozoite antigens, but instead discusses sporozoite antigens. Yang does not discuss any of the recited fragments. Instead, Yang discusses a C-terminal MSP-1 fragment that is different from any of the recited fragments. Kumar discusses use of a recombinant vaccina virus (not a recombinant MVA virus) encoding MSP-1 p42, to infect target cells for CTL analysis. For immunization, Kumar used a plasmid vector encoding MSP-1 p42. Bujard discusses a recombinant vector encoding full-length (p190) MSP-1. Thus, the cited art does not disclose the combination of elements recited in claim 1.

The Office Action stated that the teachings in the art provide those of ordinary skill in the art with a reasonable expectation of success in the use of MVA as a booster vaccine; and cited Zavala et al. ((2001) *Virology* 280:155; "Zavala").

First, Applicants note that only the first page of Zavala was provided with the Office Action. The Office Action cites pages 157-158 of Zavala. Pages 157-158 of Zavala were not provided with the Office Action.

Secondly, Zavala discusses the use of recombinant vectors as part of very narrowly defined vaccination

regimens. That is, within the framework of priming with naked DNA and subsequent boosting with recombinant DNA, Zavala teaches that the CD8+ T cell response against two separate epitopes from two different pathogens (e.g., malaria and HIV) can be enhanced. From the context of the discussion in Zavala, it is therefore clear that the "multi" in "multiepitope" refers not merely to different epitopes, but rather to different epitopes from different and unrelated pathogens. In contrast, the MSP-1 fragments expressed recited in the instant claims are all from the same larger protein associated with the same pathogen; regardless of whether the relevant epitopes are on p42, p83, p38 or p30 fragments, all are from MSP-1. The skilled person may have considered the teaching of Zavala if he were interested in simultaneously vaccinating against two separate diseases with the same vaccine; however, he would not consider such teaching relevant for the present case relating to compositions for immunizing against malaria using fragments of a single protein.

The cited art does not disclose or suggest all of the claim elements of claim 1. Furthermore, Schneider teaches away from the proposed combination. Thus, the recombinant MVA vector as claimed, or a vaccine composition comprising same, is **not** simply a predictable combination of prior art elements. As such, Schneider, alone or in combination with Yang, Kumar, and Bujard, cannot render any of claims 1, 2, and 6-18, and 22-25 obvious.

Conclusion as to the rejections under 35 U.S.C. §103(a)

Applicants submit that the rejection of claims 1, 2, and 6-18, and 22-25 under 35 U.S.C. §103(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Nonstatutory double patenting

1) Claims 1, 2, 6-18, and 20-25 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-8, 12-19, and 23-31 of U.S. Patent No. 7,198,934, or of claims 1-5, 8-11, 16-19, 24-28, 31, and 33 of U.S. Patent No. 6,440,422, "in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above." Office Action, page 11.

2) Claims 11, 12, and 18 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-8, 12-19, and 23-31 of U.S. patent No. 7,049,145 "in view of the teachings of Schneider et al. and Kumar et al. as applied above." Office Action, page 11.

3) Claims 1, 2, 6-18, and 20-25 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 5, 7, 11, and 12 of copending Application No. 11/375,159, now U.S. Patent No. 7,767,209, "in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above." Office Action, page 12.

4) Claims 1, 2, and 6-25 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 5, 7, 11, and 12 of co-ending Patent Application No 11/375,159, now U.S. Patent No. 7,767,209, "in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above." Office Action, page 12.

5) Claim 17 was were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-10 and 21-23 of copending Application No. 12/523,023 "in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above." Office Action, page 13.

First, Applicants note that claims 23 and 24 were cancelled without prejudice to renewal in the amendment, filed on November 23, 2009 and responsive to the July 21, 2009 Office Action.

Secondly, an obviousness-type double patenting analysis involves an analysis that "compares **claims** in an earlier patent to **claims** in a later patent or application." *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC,* 349 F.3d 1373 9Fed. Cir. 2003); emphasis added. The Office Action based the rejections over a combination of claims and cited art. However, it is well established that the proper analysis is a claim to claim analysis. As such, the Office Action has not made a proper analysis.

Thirdly, the Office Action has made very general statements, and has not actually provided a basis as to why any of the instant claims are allegedly obvious over the cited claims. Obviousness-type double patenting is a judicially created doctrine that prevents a later patent from **covering a slight variation** of an earlier patented invention. *Perricone v. Medicis Pharm. Corp.* 432 F.3d 1368 (Fed. Cir. 2005). The Office Action has not explained why it believes that any of the instant claims are an "obvious variation" over the cited claims.

U.S. Patent No. 7,198,934

Claim 1 of U.S. Patent No. 7,198,934 recites:

> 1. A method of expressing a foreign gene comprising
> inserting the foreign gene at a site of a naturally occurring deletion within a Modified Vaccinia Virus Ankara (MVA) genome, and
> introducing the MVA containing the foreign gene into a cell under conditions such that the foreign gene is expressed;
> wherein the site of a naturally occurring deletion within said MVA genome is selected from the group consisting of deletion site I, site II, site IV, site V, and site VI.

The Office Action has failed to provide a rationale as to why instant claim 1, which recites:

"A recombinant Modified Vaccinia Vaccine Ankara (MVA) virus comprising at least one nucleic acid coding for at least one fragment of a *Plasmodium falciparum* merozoite surface protein-1 (MSP-1), wherein the at least one fragment of MSP-1 is selected from:
i) p42;
ii) p42 and p38; and
iii) p83, p30, p42, and p38"

would be considered an "obvious variation" over claim 1 (or any of the other cited claims) of U.S. Patent No. 7,198,934.

The Office Action has failed to provide a rationale as to why any of instant claims 1, 2, 6-18, and 20-25 would be considered an "obvious variation" over claim 1 (or any of the other cited claims) of U.S. Patent No. 7,198,934.

U.S. Patent No. 6,440,522

Claim 1 of U.S. Patent No. 6,440,422 recites:

1. A recombinant Modified Vaccinia Ankara (MVA) virus containing and capable of expressing at least one foreign gene inserted at a site of a naturally occurring deletion within the MVA genome, wherein the site of the naturally occurring deletion is not site III.

The Office Action has failed to provide a rationale as to why instant claims 1, 2, 6-18, and 20-25 would be considered an "obvious variation" of Claim 1 (or any of the other cited claims) of U.S. Patent No. 6,440,422.

U.S. Patent No. 7,049,145

Claim 1 of U.S. Patent No. 7,049,145 recites:

1. MVA-knock-out-mutant, wherein the MVA ORF 050L gene or a functional part thereof has been inactivated in the viral genome.

The Office Action has failed to provide a rationale as to why instant claim 11, which recites:

"A method of production of a recombinant Modified Vaccinia Vaccine Ankara (MVA)-based virus, wherein the method comprises the steps:
a) transfecting a eukaryotic host cell with a transfer vector, wherein the transfer vector comprises a nucleic acid encoding at least one fragment of *Plasmodium falciparum* merozoite surface protein-1 (MSP-1) protein, wherein the at least one fragment of MSP-1 is selected from:
i) p42;
ii) p42 and p38; and
iii) p83, p30, p42, and p38,

wherein the nucleic acid is flanked by MVA sequences 5' and / or 3', wherein the sequences are suitable for the homologous recombination in the host cell;
b) infecting the cell from step (a) with a virus based on MVA;
c) cultivating the host cell under conditions suitable for homologous recombination; and
d) isolating the recombinant MVA-based virus"

would be considered an "obvious variation" of Claim 1 (or any of the other cited claims) of U.S. Patent No. 7,049,145.

The Office Action has failed to provide a rationale as to why instant claims 11, 12, and 18 would be considered an "obvious variation" of Claim 1 (or any of the other cited claims) of U.S. Patent No. 7,049,145.

U.S. Patent No. 7,767,209

Claim 1 of U.S. Patent no. 7,767,209 recites:

1. A MVA mutant, wherein the IL1βR coding sequence or a part thereof has been inactivated for use in immunotherapy and/or vaccination, wherein the MVA mutant further comprises DNA sequences coding for a heterologous protein derived from the group consisting of therapeutic polypeptides and polypeptides of pathogenic agents and functional parts thereof, wherein the MVA mutant leads to enhanced memory response of CD8+ cells of at least 10% compared to wild type MVA.

The Office Action has failed to provide a rationale as to why instant claims 1, 2, 6-18 and 20-25 would be considered an "obvious variation" of Claim 1 (or any of the other cited claims) of U.S. Patent No. 7,767,209.

The Office Action has failed to provide a rationale as to why instant claims 1, 2, and 6-25 would be considered an "obvious variation" of Claim 1 (or any of the other cited claims) of U.S. Patent No. 7,767,209.

U.S. Patent Application No. 12/523,023

Claim 1 of pending U.S. Patent Application No. 12/523,023 ('023) reads:

1. (Original) A composition comprising

(a) a purified fragment p83/30 of the gp190/MSP-1 protein from Plasmodium without heterologous sequences, and

(b) a purified fragment p38/42 of the gp190/MSP-1 protein from Plasmodium without heterologous sequences.

The Office Action appears to be of the position that instant claim 17, which recites:

> A method for the therapy of malaria, the method comprising administering: i) a recombinant virus according to one of claims 1, 2, and 6-9; and ii) MSP-1, or a fragment and / or a nucleic acid coding for MSP-1, or a fragment thereof, wherein the fragment of MSP-1 is selected from the fragments p83, p30, p38, p33, p19, and p42, or a combination thereof

is an "obvious variation" over claims 1-10 and 21-24 of the '023 application.

However, the Office Action has failed to provide a rationale as to why instant claim 17 would be considered an "obvious variation" over claims 1-10 and 21-24 of the '023 application.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number GRUE-004.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: August 30, 2010

By: /Paula A. Borden, Reg. No. 42,344/
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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